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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,706	01/28/2005	Verena Stangl	2958-128	7467

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EXAMINER	
BRADLEY, CHRISTINA	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
03/20/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/522,706	STANGL ET AL.	
	Examiner	Art Unit	
	Christina Marchetti Bradley	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 27-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-9 and 27-29 are pending; claims 1-6, 8, 9 and 27-29 read on the elected species MG132. The amendment filed 2/21/2008 is entered. Prosecution is reopened in this case based on the new grounds of rejection presented below.

Claim Objections

2. Claims 1-9 and 27-29 are objected to because of the following informalities: the proteasome inhibitors recited in claims 1, 6, 7 and 9 are listed in several different formats, for example: "N-carbobenzoxy-L-leucinyl-L-leucinyl-L-leucinal (also referred to as MG132 or ZLLL)" which is a chemical formula followed by the phrase "also referred to as" and the chemical name in parentheses; "clasto-lactacystin-beta-lacton (omuralid)" which is a chemical formula followed by the chemical name in parentheses; and "PS-303 (NH_2(CH-napthyl)-CONH-(CH-isobutyl)-B$(OH)_2$" which is the chemical name followed by the chemical formula in parentheses etc. For clarity, one format should be used. In addition, MG-132 is recited more that once in claim 1. In addition, the semicolon preceding PS-2 in claim 1 should be a comma to be consistent with the rest of the claim. In addition, a second closed parentheses is required after "SEQ ID NO: 5" in claim 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The rejection of claims 1-9 and 27-29 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in light of the amendment filed 2/21/2008.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-9 and 27-29 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the concentration of proteasome inhibitor. Claim 1 recites the limitation "wherein the amount is in a nanomolar range". The term nanomolar means nanomoles per liter and in this case nanomoles of protease inhibitor per liter. Neither the claims or specification indicate what the term liter is referring to. Several possibilities exist including liters of formualtion (i.e. saline, pill etc.) or liters of plasma, body, body fluid etc. Absent a clear definition of concentration in the claims and the specification, claims 1-9 and 27-29 are rendered indefinite.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-6, 8, 9 and 27-29 are rejected under 35 U.S.C. 102(b) as being unpatentable over Sherman *et al.* (U.S. Patent No. 6,096,711) in view of Lynas *et al.* (*Biorg. Med. Chem. Let.*,

1998, *8*, 373-8). Sherman *et al.* teach a method for treating pathologies such as ischemic cerebral infarction, ischemic acute renal failure, intestinal ischemia, and ischemic heart disease comprising administering a proteasome inhibitor to the patient (claims 8 and 12-15). The proteasome inhibitor taught by Sherman *et al.* for use in the method is the elected species MG132 (examples 1 and 2). In addition, Sherman *et al.* teach that the administration of a proteasome inhibitor during atherosclerotic disease of epicardial coronary arteries or myocardial infarction can minimize damage and provide a therapeutic window for surgical intervention (column 6, lines 1-12). Sherman *et al.* do not teach the use of nanomolar concentrations of MG132. Because the concentration of a drug is a result-effective variable, it would have been obvious to the skilled artisan to optimize the concentration through routine experimentation. See MPEP 2144.05. The skilled artisan would have been motivated to optimize the MG132 dose concentration in the nanomolar range based on the teaching of Lynas *et al.* that the Ki of MG132 is 4.0 nM (page 376). Sherman *et al.* does not disclose or suggest the use of the proteosome inhibitot to enhance the expression of eNos. Sherman *et al.* does not explicitly disclose this effect. However, because the active steps of the method taught by Sherman *et al.*, the administration of MG132 to patients suffering from pathologies such as ischemic cerebral infarction, ischemic acute renal failure, intestinal ischemia, and ischemic heart disease, and the chemical structure of the administered compound MG132, are identical to the claimed invention, there is a reasonable expectation that the method taught by Sherman *et al.* would meet this functional limitation. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Marchetti Bradley whose telephone number is (571)272-9044. The examiner can normally be reached on Monday-Thursday, 8 A.M. to 3 P.M.
10. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
11. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654

/Christina Marchetti Bradley/
Examiner, Art Unit 1654